EXHIBIT A

January 31, 2018

Via FedEx®

General Counsel
Corcept Therapeutics, Inc.
149 Commonwealth Drive
Menlo Park, California 94025

Managing Partner
Kilpatrick Townsend & Stockton LLP
1100 Peachtree Street NE
Atlanta, Georgia 30309

HIGHLY CONFIDENTIAL

Re: Notice of ANDA No. 211436
Mifepristone Tablets, 300 mg, With Paragraph IV Certifications Concerning U.S. Patent Nos. 8,921,348 and 9,829,495

Dear Madam or Sir:

Pursuant to § 505(j)(2)(B)(iv) of the Federal Food, Drug, and Cosmetic Act and 21 C.F.R. § 314.95, Teva Pharmaceuticals USA, Inc. ("Teva"), hereby provides the following notice concerning U.S. Patent Nos. 8,921,348 ("the '348 patent") and 9,829,495 ("the '495 patent") to Corcept Therapeutics, Inc. ("Corcept") as the apparent holder of approved New Drug Application ("NDA") No. 202107 for KORLYM® (mifepristone) tablets 300 mg, according to the records of the U.S. Food and Drug Administration ("FDA"), and as the record owner of U.S. Patent Nos. 8,921,348 and 9,829,495 according to the records of the U.S. Patent and Trademark Office ("USPTO").

As a courtesy, Teva is also providing a copy of this Notice Letter and Detailed Statement to Kilpatrick Townsend & Stockton LLP as correspondent for U.S. Patent Nos. 8,921,348 and 9,829,495.

I. Pursuant to 21 U.S.C. § 355(j)(2)(B)(iv)(I) and 21 C.F.R. § 314.95(c)(1) and/or 314.95(d), Teva advises Corcept that FDA has received an Abbreviated New Drug Application ("ANDA") from Teva for Mifepristone Tablets, 300 mg. The ANDA contains the required bioavailability and/or bioequivalence data and/or bioequivalence waiver. The ANDA was submitted under 21 U.S.C. § 355(j)(1) and (2)(A), and contains Paragraph IV certifications to obtain approval to engage in the commercial manufacture, use or sale of Mifepristone Tablets, 300 mg, before the expiration of U.S. Patent Nos. 8,921,348 and 9,829,495 which are listed in the Patent and Exclusivity Information Addendum of FDA's publication, *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the "Orange Book").

II. Pursuant to 21 C.F.R. § 314.95(c)(2), we advise you that FDA has assigned Actavis' ANDA the number 211436.

III. Pursuant to 21 C.F.R. § 314.95(c)(3), Teva states that is has received a Paragraph IV Acknowledgement Letter; ANDA Receipt for ANDA No. 211436 from the FDA.

IV. Pursuant to 21 C.F.R. § 314.95(c)(4), the established name of the proposed drug product is Mifepristone Tablets, 300 mg.

IV. Pursuant to 21 C.F.R. § 314.95(c)(5), the active ingredient, strength, and dosage form of the proposed drug product are Mifepristone Tablets, 300 mg.

V. Pursuant to 21 C.F.R. § 314.95(c)(6), Teva advises Corcept that the patents alleged to be invalid, unenforceable, and/or not infringed in the Paragraph IV certifications are U.S. Patent Nos. 8,921,348 and 9,829,495 which are listed in the Orange Book in connection with Corcept's approved NDA No. 202107 for KORLYM® (mifepristone) tablets 300 m. According to information published in the Orange Book, the patents will expire as follows:

U.S. PATENT NO.	EXPIRATION DATE
8,921,348	August 27, 2028
9,829,495	August 15, 2036

VI. Pursuant to 21 U.S.C. § 355(j)(2)(B)(iv)(II) and 21 C.F.R.§ 314.95(c)(7), attached to this letter is a detailed statement of the factual and legal bases for Teva USA's opinion that U.S. Patent Nos. 8,921,348 and 9,829,495 are not valid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Teva's product.

VII. Pursuant to 21 U.S.C § 355(j)(5)(C)(i)(III) and 21 C.F.R.§ 314.95(c)(8), attached to this notice letter is an Offer of Confidential Access to Application. As required by 21 U.S.C § 355(j)(5)(C)(i)(III), Teva offers to provide confidential access to certain information from its ANDA No. 211436 for the sole and exclusive purpose of determining whether an infringement action referred to in 21 U.S.C § 355(j)(5)(B)(iii) can be brought.

21 U.S.C. § 355(j)(5)(C)(i)(III) allows Teva to impose restrictions "as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information." That provision also grants Teva the right to redact its ANDA in response to a request for Confidential Access under this offer.

By providing this Offer of Confidential Access to the ANDA, Teva maintains the right and ability to bring and maintain a Declaratory Judgment action under 28 U.S.C. § 2201 *et seq.*, pursuant to 21 U.S.C. § 355(j)(5)(C).

Sincerely,

Fahd Majiduddin, Ph.D., Esq.
Patent Counsel – Associate Director
Teva Pharmaceuticals USA, Inc.

Enclosures: *Teva Pharmaceuticals USA, Inc.'s Detailed Statement Of The Factual And Legal Bases That U.S. Patent Nos. 8,921,348 and 9,829,495 Are Invalid, Unenforceable, Or Not Infringed*

Offer Of Confidential Access Pursuant To 21 U.S.C. § 355(j)(5)(C)(i)(III)

ABBREVIATED NEW DRUG APPLICATION NO. 211436
OFFER OF CONFIDENTIAL ACCESS
PURSUANT TO 21 U.S.C. § 355(j)(5)(C)(i)(III)

WHEREAS Teva Pharmaceuticals USA, Inc. ("Teva USA") has provided notice to Corcept Therapeutics, Inc. (hereinafter "Recipients") that Teva USA submitted to the U.S. Food and Drug Administration ("FDA") an Abbreviated New Drug Application No. 211436 for Teva USA's proposed Mifepristone Tablets, 300 mg (hereinafter referred to in whole or in part as the "ANDA"), containing Paragraph IV certifications with respect to U.S. Patent Nos. 8,921,348 and 9,829,495 ("the patents"), which is listed in the FDA Publication, "Approved Drug Products with Therapeutic Equivalence Evaluations"; and

WHEREAS this document constitutes Teva USA's Offer of Confidential Access to relevant portions of that ANDA pursuant to 21 U.S.C. § 355(j)(5)(C)(i)(III) which provides:

> The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patents that are the subject of the certifications under paragraph (2)(A)(vii)(IV) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

WHEREAS Teva USA offers to provide Recipients confidential access to the relevant portions of the ANDA subject to restrictions as to persons entitled access to, and on the use and disposition of, the ANDA; and

WHEREAS this document accompanies Teva USA's Notice and Detailed Statement under 21 U.S.C. § 355(j)(2)(B) with respect to the patents;

NOW, THEREFORE, Teva USA makes this offer:

1. Pursuant to 21 U.S.C. § 355(j)(5)(C)(i)(III), and subject to the restrictions recited in clause 2 below, Teva USA hereby provides Recipients this Offer of

Confidential Access for the sole purpose of determining whether to bring an action referred to in 21 U.S.C. § 355(j)(5)(B)(iii) with respect to the patents.

2. The right of confidential access offered herein is subject to the following restrictions as to persons entitled to access, and the use and disposition of any information accessed, pursuant to this Offer of Confidential Access:

A. **Persons Entitled to Access**: Persons entitled to access (hereinafter referred to as "Authorized Evaluators") under this Offer of Confidential Access are restricted to outside counsel from one law firm engaged by Recipients to represent Recipients and the staff of such outside counsel, including paralegal, secretarial, and clerical personnel who are engaged in assisting such counsel, provided that:

(1) Such outside counsel have been identified to Teva USA in writing;

(2) Such outside counsel do not engage, formally or informally, in any patent prosecution, or any FDA counseling, litigation or other work before or involving FDA;

(3) Within 5 business days of receiving such written identification, Teva USA has not objected, in writing, to provision of confidential access to the identified outside counsel.

B. **Materials Accessible by Authorized Evaluators**: A copy of the ANDA, redacted to remove portions of no relevance to any issue of patent infringement, will be provided for use by Authorized Evaluators.

C. **Use of the ANDA and Information in the ANDA**:

(1) Subject to paragraph 2(D)(2)(a), use of the ANDA, and all information contained therein or derived therefrom, and all notes, analyses, studies, or documents prepared by Authorized Evaluators to the extent they reflect information contained in or derived from the ANDA furnished herein, is for the sole and limited purpose of evaluating possible infringement of the patents, and for no other purpose.

(2) Authorized Evaluators shall not disclose any information contained in or derived from the ANDA or any notes, analyses, studies, or other documents to the extent that they reflect any information contained in or derived from the ANDA, to any person other than an Authorized Evaluator.

(3) Notwithstanding the provisions of subparagraphs 2(C)(1) and 2(C)(2) above, Authorized Evaluators shall be permitted to advise Recipients on whether or not to assert the patents, provided, however, that the

information contained in or derived from the ANDA is not thereby disclosed.

D. Disposition of the Information in the ANDA:

(1) If Recipients do not assert the patents against Teva USA within 45 days of receipt of the Notice and Detailed Statement (the "45-day period"), which this offer accompanies, Authorized Evaluators shall, and Recipients shall direct and ensure that Authorized Evaluators, within 30 days after the expiration of the 45-day period, destroy or send to Teva USA the portions of the ANDA provided, and all notes, analyses, studies, or other documents prepared or received by Authorized Evaluators, to the extent that they reflect information contained in or derived from the ANDA, and Recipients or Authorized Evaluators shall notify Teva USA that this has been done.

(2) Recipients agree that if Recipients assert the patents against Teva USA within the 45-day period of receipt of the Notice and Detailed Statement, which this offer accompanies:

(a) While the litigation is pending, the portions of the ANDA provided and all notes, analyses, studies, or other documents prepared or received by Authorized Evaluators, to the extent that they reflect information contained in or derived from the ANDA, shall be treated as information under the highest level of confidentiality under any protective order entered in the action brought against Teva USA. Until such a protective order is entered, subsection 2(C)(2) above continues to apply.

(b) Recipients shall direct and ensure that Authorized Evaluators destroy the portions of the ANDA provided and all notes, analyses, studies, or other documents prepared or received by Authorized Evaluators, to the extent that they reflect information contained in or derived from the ANDA, within thirty (30) days after the final determination of the action brought against Teva USA.

(3) Notwithstanding the provisions of subparagraphs 2(D)(1) and 2(D)(2) above, the Authorized Evaluators identified in subparagraph 2(A) shall be permitted to retain one copy of the portions of the ANDA provided and each note, analysis, study, or other document prepared by Authorized Evaluators, to the extent that they reflect information in the ANDA.

E. Accidental Disclosure: Should information contained in or derived from the ANDA be disclosed, inadvertently or otherwise, Recipients shall, at Recipients' earliest opportunity, contact Teva USA and identify:

(1) What has been disclosed;

(2) The individuals to whom such information has been disclosed; and

(3) Steps taken by Recipients and Authorized Evaluators to ensure the information contained in or derived from the ANDA continues to be treated pursuant to the terms of this agreement and is not further disseminated.

3. Recipients and Authorized Evaluators recognize that violation of any provision of this Offer of Confidential Access will cause irreparable injury to Teva USA, and that an adequate legal remedy does not exist. Teva USA, therefore, shall have the right, in addition to any other remedies available at law or in equity, to obtain from a court of competent jurisdiction an injunction to prohibit Recipients and Authorized Evaluators from violating the terms of this Offer of Confidential Access. It is further agreed that in such an action Teva USA is entitled to recover any and all damages, costs and expenses, including, but not limited to, all reasonable attorneys' fees, professional fees, and court costs.

4. Should any provision set forth in this Offer of Confidential Access be found by a court of competent jurisdiction to be illegal, unconstitutional, or otherwise unenforceable, the remaining provisions shall continue in full force and effect.

5. Nothing contained herein shall be construed as a grant of any license or other right to use information contained in or derived from the ANDA, except for the purpose expressly stated herein.

6. This Agreement shall be governed by the laws of the State of New Jersey, without giving effect to its conflicts of law or choice of law principles.

7. Each of Recipients, Authorized Evaluators, and Teva USA, irrevocably submit to and accept, generally and unconditionally, the exclusive personal jurisdiction of the courts of the State of New Jersey, and of the U.S. District Court for the State of New Jersey, waives its right to assert any objection or defense based on venue or forum *non conveniens*, and agrees to be bound by any judgment rendered thereby arising under or in respect of this Agreement.

8. When accepted by the parties hereto, this document shall constitute the entire agreement of the parties with respect to the subject matter herein, and may not be amended or modified except in writing executed by all of the parties.

9. An Authorized Evaluator may request access to the ANDA by executing one copy of this Confidential Access Agreement where indicated and returning the executed copy within the 45-day period to:

James Mahanna
Senior Counsel, Associate General Counsel, US Generics IP
Teva Pharmaceuticals USA, Inc.

200 Elmora Avenue
Elizabeth, NJ 07202
908.659.2510
jim.mahanna@actavis.com

Thereupon, the terms contained in this document shall be considered an enforceable contract between Teva USA and the Recipients.

TEVA Pharmaceuticals USA, Inc.
By its authorized agent:

_____
[Lawyer's Name]
[Firm Name if applicable]

Date: [Date]_____

Recipients
By their authorized agent(s):

Signature: _____

Name (Print): _____

Title: _____

Company: _____

Date: _____

HIGHLY CONFIDENTIAL

Enclosure

Teva Pharmaceuticals USA, Inc.'s Detailed Factual and Legal Basis for Its Paragraph IV Certification that U.S. Patent Nos. 8,921,348 and 9,829,495 Are Invalid, Unenforceable and/or Not Infringed by the Mifepristone Tablets, 300 mg Product Described in Teva Pharmaceuticals USA, Inc.'s ANDA No. 211436

I. INTRODUCTION

This document is the detailed factual and legal basis ("Detailed Statement") for Teva Pharmaceuticals USA, Inc.'s ("Teva") certification that, in its opinion and to the best of its knowledge, U.S. Patent Nos. 8,921,348 (hereinafter "the '348 patent") and 9,829,495 ("the '495 Patent") are invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, or sale of the drug products described in Teva's ANDA. The right to raise additional noninfringement, invalidity, and unenforceability defenses is expressly reserved.

II. TEVA'S ANDA PRODUCT

Teva's ANDA Product consists of Mifepristone as the active pharmaceutical ingredient in tablets, 300 mg. The proposed labeling submitted as part of Teva's ANDA is identical in all relevant respects to the labeling for KORLYM®.

The composition of Teva's ANDA Product may be disclosed pursuant to the terms set forth in the Offer of Confidential Access indicated in Teva's Notice Letter.

III. THE ORANGE BOOK LISTED PATENTS

U.S. PATENT NO.	EXPIRATION DATE
8,921,348	August 27, 2028
9,829,495	August 15, 2036

IV. LEGAL PRINCIPLES

A. Validity

The invalidity discussion below sets forth the basic legal principles considered for this detailed statement. Although an issued United States patent carries a presumption of validity, an accused infringer may succeed in showing that an issued patent is invalid by providing clear and convincing evidence of invalidity.[1] Any one of several reasons may invalidate a patent. These

[1] A court gives due weight to a patent's presumed validity under 35 U.S.C.S. § 282, requiring an accused infringer to prove invalidity by clear and convincing evidence. *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368 (Fed. Cir. 2005).

include lack of novelty, a statutory bar to patentability, obviousness, or lack of adequate disclosure. For example, an issued patent may be found invalid for failing to comply with one or more statutory requirements enumerated under 35 U.S.C. §§ 101, 102, 103, or 112.

1. Claim Construction

A proper determination of validity requires a determination of the scope of the claim elements. The same claim construction governs for validity determinations as for infringement determinations. *Door-Master Corp. v. Yorktowne, Inc.*, 256 F.3d 1308, 1312 (Fed. Cir. 2001). "Courts have the power and obligation to construe as a matter of law the meaning of language used in patent claims." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995).

Claim construction begins with an inquiry into the plain and ordinary meaning of the claim terms, which define the scope of the right to exclude. *See SkinMedica, Inc. v. Histogen Inc.*, 727 F.3d 1187, 1195 (Fed. Cir. 2013)(*citing Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005))(recognizing the ordinary meaning of a claim term as providing "an objective baseline from which to begin claim interpretation"). "When construing patent claims, there is a heavy presumption that the language in the claim carries its ordinary and customary meaning amongst artisans of ordinary skill in the relevant art at the time of the invention." *See Biogen Idec, Inc. v. GlaxoSmithKline LLC*, 713 F.3d 1090, 1095 (Fed. Cir. 2013); *see also Housey Pharm., Inc. v. Astrazeneca UK Ltd.*, 366 F.3d 1348, 1352 (Fed. Cir. 2004) (citations and internal quotation marks omitted).

In construing the meaning of claim terms, a court may consider intrinsic evidence, the claims themselves, the specification, and the prosecution history, and extrinsic evidence, *i.e.*, dictionaries, treatises, expert testimony. *Vitronics Corp. v. Conceptronics, Inc.*, 39 USPQ2d 1573 (Fed. Cir. 1996); *Markman v. Westview Instruments*, 38 USPQ2d 1461, 1463 (S. Ct. 1996); and *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398, 1409 (Fed. Cir. 1997). The claims, the specification, and, to a lesser degree, the prosecution history, are the primary focus of claim construction, while extrinsic evidence may only be used to construe a claim if the extrinsic evidence "does not contradict any definition found in or ascertained by a reading of the patent documents." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1323 (Fed. Cir. 2005). The Supreme Court has held that a district court's analysis of the intrinsic evidence and its ultimate determination as to the proper meaning of the claim are reviewed *de novo*, while its fact findings regarding extrinsic evidence are given deference and reviewed for clear error. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831 (2015).

Generally, patent claims, "...are to receive a liberal construction, and under the fair application of the rule, *ut res magis valeat quam pereat*, are, if practicable, to be so interpreted as to uphold and not to destroy the right of the inventor." *Turrill v. Mich. S. & N. Ind. R. R.*, 68 U.S. 491, 510 (1863). However, there are limits to liberal claim construction. For example, claims may be considered broad "to the point of invalidity" if the properly constructed claim scope includes significant numbers of inoperative embodiments. *See, e.g., Graver Tank & Mfg. Co. v. Linde Air Products Co.*, 336 U.S. 271, 276-77 (1949).

Conversely, claim language should not be limited simply to render the claim valid:

> "If the only claim construction that is consistent with the claim's language and the written description renders the claim invalid, then the axiom does not apply and the claim is simply invalid." In cases where the patent claims are substantially overreaching, it would be inappropriate for the construing court to rewrite the claims to preserve validity. Thus it is not proper for the court to put the validity cart before the claim construction horse."

Rhine v. Casio, Inc., 183 F.3d 1342, 1345 (Fed. Cir. 1999). *See also*, *Nazomi Communs., Inc. v. Arm Holdings, PLC*, 403 F.3d 1364, 1369 (Fed. Cir. 2005).

Further, where the patent specification makes clear that prior art techniques are not part of the invention, a claim construction that excludes such techniques is correct. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1319 (Fed. Cir. 2005).

2. Anticipation

The various paragraphs of 35 U.S.C. § 102 set forth the conditions that preclude an applicant from receiving a patent for lack of novelty, and define what information or events are deemed "prior art" against a particular invention. Section 102(a) bars patentability of an invention if it was "known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent." 35 U.S.C. § 102(a). The statute also bars patentability if the invention was "patented or described in a printed publication in this or a foreign country . . . more than one year prior to the date of the application for patent in the United States." 35 U.S.C. § 102(b). "In order to qualify as a printed publication within the meaning of § 102, a reference must have been sufficiently accessible to the public interested in the art." *In re Lister*, 583 F.3d 1307, 1311 (Fed. Cir. 2009) (internal citation and quotation marks omitted). A reference is considered publicly accessible if it was "disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art exercising reasonable diligence, can locate it." *Kyocera Wireless Corp. v. Int'l Trade Comm'n*, 545 F.3d 1340, 1350 (2008) (internal citation and quotation marks omitted).

"Under 35 U.S.C. § 102, a claim is anticipated if each and every limitation is found either expressly or inherently in a single prior art reference." *See King Pharm., Inc. v. Eon Labs., Inc.*, 616 F.3d 1267, 1274 (Fed. Cir. 2010) (internal citation and quotation marks omitted); *see also ClearValue, Inc. v. Pearl River Polymers, Inc.*, 668 F.3d 1340, 1344 (Fed. Cir. 2012). While the anticipating reference must be enabling, *Am. Calcar, Inc. v. Am. Honda Motor Co.*, 651 F.3d 1318, 1341 (Fed. Cir. 2011), additional references and extrinsic evidence can be used to show the reference contains an enabled disclosure. *In re Donohue*, 766 F.2d 531, 534 (Fed. Cir. 1985); *In re Samour*, 571 F.2d 559, 562 (C.C.P.A. 1978) ("[T]he disclosure . . . must be considered together with the knowledge of one of ordinary skill in the pertinent art."). Additional references or other evidence also can be used to show meaning of a term used in the primary reference. *In re Baxter Travenol Labs.*, 952 F.2d 388, 390 (Fed. Cir. 1991).

The classic test for anticipation is often stated in terms of an infringement analysis, namely, "[t]hat which would literally infringe if later in time anticipates if earlier than the date of invention." *Ecolab, Inc. v. FMC Corp.*, 569 F.3d 1335, 1348 (Fed. Cir. 2009) (quoting *Lewmar Marine, Inc. v. Barient, Inc.*, 827 F.2d 744, 747 (Fed. Cir. 1987), *cert. denied*, 484 U.S. 1007 (1988)). Thus, a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including non-preferred embodiments. *Celeritas Techs. Ltd. v. Rockwell Int'l Corp.*, 150 F.3d 1354, 1361 (Fed. Cir. 1998) (holding that the prior art anticipated the claims even though it taught away from the claimed invention); *Merck & Co. v. Biocraft Labs.*, 874 F.2d 804 (Fed. Cir. 1989), *cert. denied*, 493 U.S. 975 (1989); *ArcelorMittal France v. AK Steel Corp.*, 700 F.3d 1314, 1322 (Fed. Cir. 2012).

"Moreover, a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference." *Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (citation omitted); *see also Allergan, Inc. v. Apotex Inc.*, 754 F.3d 952, 958 (Fed. Cir. 2014). The Federal Circuit has explained that the standard of certainty required for inherent anticipation is not whether a party can prove by clear and convincing evidence that the claimed invention existed in the prior art as an absolute certainty, but rather "merely that the disclosure is sufficient to show that the natural results flowing from the operation as taught would result in the claimed product." *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343 (Fed. Cir. 2005) (internal citation and quotation marks omitted). Additional references or evidence can be used to show that a person of ordinary skill in the art would recognize the inherent characteristic of the thing taught by the primary reference. *E.g.*, *Teleflex, Inc.*, 299 F.3d at 1335 (recognizing that courts permit "the use of additional references to confirm the contents of the allegedly anticipating reference"); *Cont'l Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991); *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991) *overruled on other grounds by Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1293 (Fed. Cir. 2009), *cert. denied,* 558 U.S. 1136 (2010) ("The role of extrinsic evidence is to educate the decision-maker to what the reference meant to persons of ordinary skill in the field of the invention, not to fill gaps in the reference."). Inherent anticipation, however, "does not require a person of ordinary skill in the art to recognize the inherent disclosure in the prior art at the time the prior art is created." *SmithKline Beecham*, 403 F.3d at 1343; *see also Abbott Labs. v. Baxter Pharm. Prods., Inc.*, 471 F.3d 1363, 1367 (Fed. Cir. 2006) ("[A] reference may anticipate even when the relevant properties of the thing disclosed were not appreciated at the time.").

3. Obviousness

A claim may be shown to be obvious in view of the prior art. Although the ultimate determination of obviousness under § 103 is a question of law, the evaluation is based on several underlying factual factors, often referred to as "the Graham factors," including: "(1) the scope and content of the prior art; (2) the level of ordinary skill in the pertinent art; (3) the differences between the claimed invention and the prior art; and (4) evidence of secondary factors, such as commercial success, long-felt need, and the failure of others."

Often invalidity is also established in view of the elements for establishing a *prima facie* case of obviousness. A showing of statutory obviousness generally has three requirements:

1. A combination of two or more prior art references must teach or suggest all claim limitations of the rejected claim(s).[2, 3, 4]

2. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings.[5]

3. One of ordinary skill in the art must have a reasonable expectation of success in combining the references.[6, 7]

As mentioned above, "[i]n making the assessment of differences between the prior art and the claimed subject matter, § 103 specifically requires consideration of the claimed invention "as a whole." The reason for this is that virtually all inventions are combinations of old elements and it is almost always possible to deconstruct the invention into all of its individual elements. *Envtl. Designs, Ltd. v. Union Oil Co.*, 713 F.2d 693, 698 (Fed. Cir. 1983). The aforementioned rule is further supported by the recent decision in *KSR. KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (U.S. 2007).

> "[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known."

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[2] A reference that "covers the steps" between what was disclosed in the prior art and what is claimed in a patent supports a finding of obviousness.

[3] Where a problem is within the knowledge of one of ordinary skill in the art, it is irrelevant for purposes of determining obviousness that the relevant prior art does not disclose the problem. *Cross Medical Products, Inc. v. Medtronic Sofamor Danek Inc. and Medtronic Sofamor Danek USA, Inc.*, 424 F.3d 1293, 1323 (Fed. Cir. 2005).

[4] *In re Royka*, 490 F.2d 981(CCPA 1974).

[5] *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988).

[6] The expectation of success must be found in the prior art, and not in the patent specification at issue.

[7] *In re Vaeck*, 947 F.2d 488, 490 (Fed. Cir. 1991).

Id. at 1741.

The *KSR* decision indicates that pressure to solve a known problem, the presence of a limited number of predictable solutions, and anticipated success are all relevant factors in determining whether an invention is obvious. The inquiry may be referred to as the "common sense" standard, and is described below.

> "When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103. . . . Rigid preventative rules that deny fact finders recourse to common sense, however, are neither necessary under our case law nor consistent with it."

Id. at 1743.

The common sense standard provides that the motivation to combine references may be present in the nature of the problem to be solved or known by one of skill in the art. Nevertheless, the proper legal frame of reference for any obviousness inquiry is to assess the invention "as a whole" to prevent evaluation of the invention part by part. Without this important requirement, an obviousness assessment might successfully break an invention into its component parts, then find a prior art reference corresponding to each component. Further, this improper method would discount the value of combining various existing features or principles in a new way to achieve a new result-often the essence of invention." *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 411 F.3d 1332, 1337 (Fed. Cir. 2005).

a. Secondary Considerations of Non-Obviousness

It is well established that evidence of secondary indicia of nonobviousness may be asserted to overcome a *prima facie* case of obviousness. The Supreme Court has instructed that while evidence of secondary considerations can tip the balance into finding that an invention is not obvious, the secondary considerations cannot of themselves trump a clear showing that the invention is obvious. In *Dow Chemical Co. v. Halliburton Oil Well Cementing Co.*, 324 U.S. 320, 330 (1945), the Supreme Court held that "[secondary] considerations are relevant only in a close case where all other proof leaves the question of invention in doubt. Here the lack of invention is beyond doubt and cannot be outweighed by such factors [of long felt need and commercial success]." *Id.*

The Federal Circuit has provided similar holdings, finding that the presence of secondary considerations, such as surprising/unexpected results and commercial success, even if established, may not be sufficient to overcome a strong case of *prima facie* obviousness. In *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1372 (Fed. Cir. 2007), the Federal Circuit rejected the

patentee's evidence of unexpected results, but noting that even if the results were unexpected, that showing would not trump the clear case of obviousness—"[W]e hold that even if Pfizer showed that amlodipine besylate exhibits unexpectedly superior results, this secondary consideration does not overcome the strong showing of obviousness in this case. Although secondary considerations must be taken into account, they do not necessarily control the obviousness conclusion. Here, the record establishes such a strong case of obviousness that Pfizer's alleged unexpectedly superior results are ultimately insufficient." *Id.*

In *Allergan, Inc. v. Sandoz Inc.*, 106 U.S.P.Q.2d 1574, 2013 WL 1810852, *7 (Fed. Cir. 2013), the Federal Circuit reversed a finding of validity, and ruled that claims directed to a composition comprising about 0.2% timolol and about 0.5% brimonidine as the sole active agents, and used to treat glaucoma in a twice-a-day application to improve patient compliance, were invalid where the prior taught the use of the two constituents in a serial application. The Federal Circuit found that, while the twice-a-day application was an unexpected result, it was not sufficient to overcome the conclusion of obviousness based on the prior art. The Court explained that there was extensive evidence in the prior art showing the concomitant administration of brimonidine and timolol multiple times per day, that the combination had benefits over the administration of either alone, and that there was a motivation to combine the two to achieve better patient compliance. In view of this, the Federal Circuit concluded that regardless of whether the combination also solved problems associated with the afternoon trough, the motivation to make the combination was real, and held that the claims of the patent at issue were invalid as obvious.

Further, in *Richardson-Vicks Inc. v. Upjohn Co.*, 122 F.3d 1476, 1484 (Fed. Cir. 1997), the Federal Circuit held a patent invalid as obvious where the patent was directed to a composition and method of use claims that combined a dose of ibuprofen and pseudoephedrine into a single tablet with a specific ratio range. Prior to the invention, doctors routinely prescribed these drugs simultaneously but in separate tablets, and other prior art tablets existed containing the combination of an analgesic with pseudoephedrine. Therefore, despite evidence of unexpected results that the combination into a single tablet produced an unexpected synergy, and the commercial embodiment enjoyed commercial success, the Federal Circuit held that these secondary considerations did not overcome the strong showing of obviousness based on the prior art.

B. Infringement

To literally infringe a United States Letters Patent, an accused product or process must meet each and every limitation of the patent claim exactly, including any functional limitations. *See Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1258 (Fed. Cir. 1989). Any deviation from the claim precludes a finding of literal infringement. *See, e.g., Cole v. Kimberly-Clark Corp.*, 102 F.3d 524, 532 (Fed. Cir. 1996).

An analysis of literal infringement requires two inquiries: first, the claims must be construed to resolve their proper scope and meaning; and second, it must be determined whether the accused product or process falls exactly within the scope of the properly construed claims. *See Markman*, 52 F.3d at 976; *see also Novo Nordisk of N. Am., Inc. v. Genentech, Inc.*, 77 F.3d

1364, 1368 (Fed. Cir. 1996). The first inquiry is a legal question for the court; the second inquiry is a factual determination for the fact-finder. *See Markman*, 52 F.3d at 976–80.

Infringement may also be found under the doctrine of equivalents if the accused product or method includes features that are equivalent to each claimed element. *Warner-Jenkinson Co., Inc. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21, 40 (1997). The determination of equivalency, which is evaluated as of the time of infringement, is an objective inquiry applied on an element-by-element basis taking into account the role of each claim element in the context of the claim. *Id.* at 29, 40.

The Supreme Court has not mandated any specific approach to evaluate equivalency. *Id.* at 39-40. Among the recognized approaches that may be applied include the function-way-result test and the insubstantial differences test. *Id.* at 25, 36, 39-40.

There are a number of limitations on the application of the doctrine of equivalents. For example, the doctrine of equivalents cannot be applied so as to effectively eliminate a claim limitation in its entirety. *Id.* at 29. Further, limitations may not be afforded a scope of equivalency that effectively results in a claim that does not patentably distinguish the prior art. *See, e.g., Wilson Sporting Goods Co. v. David Geoffrey & Assocs.*, 904 F.2d 677, 683 (Fed. Cir. 1990), overruled on other grounds by *Cardinal Chem. Co. v. Morton Int'l*, 508 U.S. 83 (1993). Additionally, prosecution history estoppel operates to prevent recapture, through the doctrine of equivalents, of coverage of subject matter that was relinquished by amendment or argument during prosecution. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 535 U.S. 722, 733-34 (2002).

Although the sale of an apparatus to perform a patented method or process is not a direct infringement of a method or process claim, such a sale may nevertheless constitute an active inducement of infringement under 35 U.S.C. § 271(b) and/or a contributory infringement under 35 U.S.C. § 271(c). *See Joy Techs., Inc. v. Flakt, Inc.*, 6 F.3d 770, 774 (Fed. Cir. 1993). "Liability for either active inducement of infringement or for contributory infringement is dependent upon the existence of direct infringement." *Id.*; *see also C.R. Bard, Inc. v. Advanced Cardiovascular Sys., Inc.*, 911 F.2d 670, 673 (Fed. Cir. 1990).

Inducement of infringement is actively and knowingly aiding and abetting another's direct infringement of a patent claim. *See id.* at 675; *DSU Med. Corp. v. JMS Co., Ltd.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006). In order to find induced infringement, a patentee must show (i) direct infringement, either literally or under the doctrine of equivalents, (ii) that the alleged indirect infringer actually intended to cause another to directly infringe, (iii) that the alleged indirect infringer knew of the allegedly infringed patents, and (iv) that the alleged indirect infringer knew or should have known that its actions would lead to actual infringement. *See* 35 U.S.C. § 271(b) (2011); *see also, Commil USA, LLC v. Cisco Systems, Inc., No. 13-896* (S. Ct., May 26, 2015); *DSU Med. Corp.*, 471 F.3d at 1304–05.

Contributory infringement is knowingly making and/or selling a product for use in practicing a patented method or process, when that product is specifically designed for use in

infringement of the patented method or process and has no substantial non-infringing uses. *See Preemption Devices, Inc. v. Minn. Mining & Mfg. Co.*, 803 F.2d 1170, 1174 (Fed. Cir. 1986).

Finally, "an invalid patent cannot be infringed, or that someone cannot be induced to infringe an invalid patent, is in one sense a simple truth, both as a matter of logic and semantics." *Commil USA, LLC v. Cisco Systems, Inc.*, 135 S. Ct. 1920, 1929 (2015) (*citing M. Swift & Sons, Inc. v. W.H. Coe Mfg. Co.*, 102 F.2d 391, 396 (C.A.1 1939). In other words, "if at the end of the day, an act that would have been an infringement or an inducement to infringe pertains to a patent that is shown to be invalid, there is no patent to be infringed." *Id.*

V. FACTUAL AND LEGAL BASIS FOR TEVA'S CERTIFICATION FOR U.S. PATENT NO. 8,921,348

A. U.S. Patent No. 8,921,348 – "Optimizing mifepristone levels in plasma serum of patients suffering from mental disorders treatable with glucocorticoid receptor antagonists"

The '348 patent, entitled "Optimizing Mifepristone Levels in Plasma Serum of Patients Suffering From Mental Disorders Treatable With Glucocorticoid Receptor Antagonists," issued on December 30, 2014, from Application Serial No. 14/065,792 ("the '792 application"), filed on October 29, 2013, which is a continuation of Application Serial No. 12/199,114 ("the '114 application"), filed on August 27, 2008, now U.S. Patent No. 8,598,149 ("the '149 patent"), which claims the benefit of U.S. Provisional Application Serial No. 60/969,027, filed on August 30, 2007.

The '348 patent issued with 7 claims, with claim 1 being the sole independent claims

The claims of the '348 patent recite:

> 1. A method for optimizing levels of mifepristone in a patient suffering from a disorder amenable to treatment by mifepristone, the method comprising: treating the patient with seven or more daily doses of mifepristone over a period of seven or more days; testing the serum levels of the patient to determine whether the blood levels of mifepristone are greater than 1300 ng/mL; and adjusting the daily dose of the patient to achieve mifepristone blood levels greater than 1300 ng/mL.
>
> 2. The method of claim 1, wherein the disorder is a member selected from the group consisting of a stress disorder, delirium, mild cognitive impairment (MCI), dementia, psychosis and psychotic major depression.
>
> 3. The method of claim 2, wherein the stress disorder is a member selected from the group consisting of Acute Stress Disorder, Post-Traumatic Stress Disorder and Brief Psychotic Disorder with Marked Stressor(s).
>
> 4. The method of claim 1, wherein each of the seven or more daily doses of mifepristone are administered orally.

5. The method of claim 1, wherein the patient is treated with 28 or more daily doses over a period of 28 or more days.

6. The method of claim 1, wherein the testing is performed by a plasma sampling collection device suitable for detecting mifepristone serum levels.

7. The method of claim 1, wherein the adjusting step comprises increasing the daily dose of the patient to achieve mifepristone blood levels greater than 1300 ng/mL.

B. Claim Construction

For the purposes of this Detailed Statement only, the claims of the '348 patent are to be accorded their ordinary and customary meanings to one of ordinary skill in the art as informed by the specification and prosecution history.

C. Non-Infringement Analysis

1. Claims 1 through 7 of the '348 Patent are Not Infringed

Teva's ANDA Product will not, infringe the claims of the '348 patent, either literally or under the doctrine of equivalents.

2. Independent Claim 1

a) No Direct Infringement

Teva's ANDA Product will not directly infringe independent claim 1 of the '348 patent. An accused product or process literally infringes a claim only if it possesses each and every limitation of the claim. If an accused product or process lacks even one claim element, it does not literally infringe the claim. *Cross Med. Prods., Inc. v. Medtronic Sofamor Danek, Inc.*, 424 F.3d 1293, 1310 (Fed. Cir. 2005). Teva's ANDA Product will not directly infringe independent claim 1 of the '348 patent because claim 1 requires "treating a patient" and Teva through its ANDA will not be treating patients. Teva's ANDA Product will not directly infringe independent claim 1 of the '348 patent for the additional reason that claim 1 requires "testing the serum levels of the patient to determine whether the blood levels of mifepristone are greater than 1300 ng/mL" and Teva through its ANDA will not test the serum levels of mifepristone in patients. Because Teva will not treat patients and does not test the serum levels of mifepristone in patients, Teva's ANDA Product will not literally infringe independent claim 1 of the '348 patent.

Furthermore, because Teva through its ANDA will not treat patients and will not test the serum levels of mifepristone in patients, Teva through its ANDA will not infringe independent claim 1 of the '348 patent under the doctrine of equivalents. The doctrine of equivalents does not allow a claim limitation to be ignored. *Pennwalt Corp. v. Durand-Wayland, Inc.*, 833 F.2d 931, 935 (Fed. Cir. 1987); *see also Novartis Pharms. Corp. v. Eon Labs Mfg., Inc.*, 363 F.3d 1306, 1312 (Fed. Cir. 2004). Because Teva through its ANDA will not treat patients and will not

test the serum levels of mifepristone in patients, Teva will not, directly infringe independent claim 1 of the '348 patent, either literally or under the doctrine of equivalents.

b) No Inducement of Infringement

The proposed labeling for Teva's ANDA Product will not induce infringement of independent claim 1 of the '348 patent. As discussed above, claim 1 requires "testing the serum levels of the patient to determine whether the blood levels of mifepristone are greater than 1300 ng/mL." Claim 1 further requires "adjusting the daily dose of the patient to achieve mifepristone blood levels greater than 1300 ng/mL." The labeling for Teva's ANDA Products (like the labeling for Korlym®), however, does not include any instructions directing a person to test (*i.e.*, determine (*see* the '348 patent at col. 6, lines 3-6)) the serum levels of the patient to determine the blood levels of mifepristone, much less to determine if the blood levels of mifepristone are greater than 1300 ng/mL and to adjust the daily dose of the patient to achieve mifepristone blood levels greater than 1300 ng/mL. Rather, the proposed labeling for Teva's ANDA Product simply instructs that mifepristone is administered at a starting dose of 300 mg, orally, once daily and can be increased. Specifically, the labeling for Korlym® states:

> **1 INDICATIONS AND USAGE**
>
> KORLYM (mifepristone) is a cortisol receptor blocker indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery.
>
> LIMITATIONS OF USE:
>
> • KORLYM should not be used in the treatment of patients with type 2 diabetes unless it is secondary to Cushing's syndrome.
>
> **2 DOSAGE AND ADMINISTRATION**
>
> **2.1 Adult Dosage**
>
> The recommended starting dose is 300 mg orally once daily. KORLYM must be given as a single daily dose. KORLYM should always be taken with a meal. Patients should swallow the tablet whole. Do not split, crush, or chew tablets.
>
> Dosing and titration
>
> The daily dose of KORLYM may be increased in 300 mg increments. The dose of KORLYM may be increased to a maximum of 1200 mg once daily but should not exceed 20 mg/kg per day. Increases in dose should not occur more frequently than once every 2-4 weeks. Decisions about dose increases should be based on a clinical assessment of tolerability and degree of improvement in Cushing's syndrome manifestations. Changes in glucose control, anti-diabetic medication requirements, insulin levels, and psychiatric symptoms may provide an early assessment of response (within 6 weeks) and may help guide early dose titration. Improvements in cushingoid appearance, acne, hirsutism, striae, and body weight occur over a longer period of time and, along with measures of glucose control,

> may be used to determine dose changes beyond the first 2 months of therapy. Careful and gradual titration of KORLYM accompanied by monitoring for recognized adverse reactions (See Warnings and Precautions 5.1 and 5.2) may reduce the risk of severe adverse reactions. Dose reduction or even dose discontinuation may be needed in some clinical situations. If KORLYM treatment is interrupted, it should be reinitiated at the lowest dose (300 mg). If treatment was interrupted because of adverse reactions, the titration should aim for a dose lower than the one that resulted in treatment interruption.

(Korlym® Prescribing Information at page 2).

Labeling that merely directs a person to administer mifepristone to "control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery" at a starting does of 300 mg once daily that can be titrated to 1200 mg once daily with no instructions to "test[] the serum levels of the patient to determine whether the blood levels of mifepristone are greater than 1300 ng/mL [or to] adjust[] the daily dose of the patient to achieve mifepristone blood levels greater than 1300 ng/mL" does not induce infringement of a method claim that requires testing the serum levels. *See Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1364 (Fed. Cir. 2003); *Allergan, Inc. v. Alcon Laboratories, Inc.*, 324 F.3d 1322 (Fed.Cir.2003); and *Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316 (Fed. Cir. 2012). Indeed, the labeling states that "[d]ecisions about dose increases should be based on a clinical assessment of tolerability and degree of improvement in Cushing's syndrome manifestations" (Korlym® Prescribing Information at page 2, emphasis added), rather than mifepristone blood levels.

The proposed labeling for Teva's ANDA Product will also not induce infringement of dependent claims 2 and 3 of the '348 patent for the additional reason that the proposed labeling for Teva's ANDA Product does not direct a person to administer mifepristone to treat "stress disorder, delirium, mild cognitive impairment (MCI), dementia, psychosis and psychotic major depression." The proposed labeling does not include any instructions that mifepristone should be administered to treat any of these conditions. Rather, as discussed above, the only indication that will be included in the proposed labeling for Teva's ANDA Product will be the same as the indication included in the labeling for KORLYM®. Labeling that merely directs a person to administer mifepristone to "control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery" does not induce infringement of a method claim that requires treating stress disorder, delirium, mild cognitive impairment (MCI), dementia, psychosis or psychotic major depression. *See Warner-Lambert Co.*, 316 F.3d at 1364; *Allergan, Inc.*, 324 F.3d at 1322; and *Bayer Schering*, 676 F.3d at 1316.

Accordingly, the proposed labeling for Teva's ANDA Product will not induce infringement of independent claim 1 and dependent claims 2 and 3 of the '348 patent.

c) No Contributory Infringement

Further, the Teva would not be liable for contributory infringement of the claims of the '348 patent because Teva's ANDA Product would be a staple article of commerce clearly suitable for substantial uses that would not infringe the claims of the '348 patent, namely administering mifepristone "to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery" without "testing the serum levels of the patient to determine whether the blood levels of mifepristone are greater than 1300 ng/mL; and adjusting the daily dose of the patient to achieve mifepristone blood levels greater than 1300 ng/mL."

3. Dependent Claims 2-7

Claims 2-7 depend directly or indirectly from claim 1. Teva's ANDA Product will not infringe dependent claims 2-7, either literally or under the doctrine of equivalents, at least by virtue of their dependence on claim 1. *Wahpeton Canvas Co. v. Frontier, Inc.*, 870 F.2d, 1546, 1552 (Fed. Cir. 1989) ("It is axiomatic that dependent claims cannot be found to be infringed unless the claims from which they depend have been found to have been infringed").

4. Conclusions Regarding Non-Infringement

Accordingly, for the reasons set forth above, Teva's ANDA Product will not infringe the claims of the '348 patent, either literally or under the doctrine of equivalents.

VI. FACTUAL AND LEGAL BASIS FOR TEVA'S CERTIFICATION FOR U.S. PATENT NO. 9,829,495

A. U.S. Patent No. 9,829,495 – "Methods for Differentially Diagnosing ACTH-Dependent Cushing Syndrome"

U.S. Patent No. 9,829,495 ("the '495 patent"), entitled "Methods for Differentially Diagnosing ACTH-Dependent Cushing Syndrome," issued on November 28, 2017, from Application Serial No. 15/236,015 ("the '015 application"), filed on August 12, 2016, which claims the benefit of U.S. Provisional Application Serial No. 62/204,723, filed on August 13, 2015.

The '495 patent issued with 18 claims of which claims 1 and 18 are independent. Independent claims 1 and 18 recite:

> 1. A method of concurrently treating Cushing's syndrome and differentially diagnosing adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome in a patient where the differential diagnosis is between ectopic ACTH syndrome and Cushing's disease, the method comprising the steps of:
>
> (i) selecting a patient with Cushing's syndrome and also elevated ACTH levels;

(ii) administering a dose of glucocorticoid receptor antagonist (GRA) sufficient to increase ACTH from the pituitary gland by at least two fold in persons with normal Hypothalamus Pituitary Adrenal (HPA) function;

(iii) waiting for at least two hours; and,

(iv) obtaining from the patient an ACTH concentration ratio wherein the ratio is derived from the ACTH concentrations in fluid obtained from either the left or right inferior petrosal venous sinus and from fluid obtained from a periphery venous sample;

wherein an ACTH concentration ratio of greater than 3 for the ACTH concentration from the inferior venous sinus sample over the periphery venous sinus sample is diagnostic of Cushing's disease.

18. A method of concurrently treating Cushing's syndrome and obtaining a measurement indicative of differential diagnosis of adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome in a patient where the differential diagnosis is between ectopic ACTH syndrome and Cushing's disease, the method comprising the steps of:

determining the ACTH concentration ratio from a patient with Cushing's syndrome and an elevated ACTH level,

where the patient has been administered a dose of glucocorticoid receptor antagonist (GRA) at least two hours prior to the removal of venous samples and

where the amount of GRA administered to the patient is sufficient to increase ACTH from the pituitary gland by at least two fold in persons with normal Hypothalamus Pituitary Adrenal (HPA) function;

wherein the ACTH concentration ratio is derived from the ACTH concentrations in fluid obtained from either the left or right inferior petrosal venous sinus and from fluid obtained from a periphery venous sample; and

wherein an ACTH concentration ratio of greater than 3 for the ACTH concentration from the inferior venous sinus sample over the periphery venous sinus sample is indicative of Cushing's disease.

Claims 2-17 depend directly or indirectly from claim 1 and further limit the periphery venous sample or the glucocorticoid receptor antagonist.

B. Claim Construction

For the purposes of this Detailed Statement only, the claims of the '495 patent are to be accorded their ordinary and customary meanings to one of ordinary skill in the art as informed by the specification and prosecution history.

C. Non-Infringement Analysis

Teva's ANDA Product will not infringe the claims of the '495 patent, either literally or under the doctrine of equivalents.

1. No Literal Infringement

Teva's ANDA Product will not directly infringe independent claims 1 and 18 of the '495 patent because Teva's ANDA Product will not meet each and every limitation of these claims. An accused product or process literally infringes a claim only if it possesses each and every limitation of the claim. If an accused product or process lacks even one claim element, it does not literally infringe the claim. *Cross Med. Prods., Inc. v. Medtronic Sofamor Danek, Inc.*, 424 F.3d 1293, 1310 (Fed. Cir. 2005); *Pennwalt Corp. v. Durand-Wayland, Inc.*, 833 F.2d 931, 935 (Fed. Cir. 1987) ("each element of a claim is material and essential, and that in order for a court to find infringement, the plaintiff must show the presence of every element or its substantial equivalent in the accused device" (*quoting Lemelson v. United States,* 752 F.2d 1538, 1551 (Fed. Cir. 1985)); and *Novartis Pharms. Corp. v. Eon Labs Mfg., Inc.*, 363 F.3d 1306, 1312 (Fed. Cir. 2004) ("[t]he doctrine of equivalents is not a license to ignore claim limitations" (*citing Dolly, Inc. v. Spalding & Evenflo Cos., Inc.*, 16 F.3d 394, 398 (Fed. Cir. 1994)).

Independent claim 1 is directed to a "method of concurrently treating Cushing's syndrome and differentially diagnosing adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome in a patient where the differential diagnosis is between ectopic ACTH syndrome and Cushing's disease." The method requires the steps of:

> (i) selecting a patient with Cushing's syndrome and also elevated ACTH levels;
>
> (ii) administering a dose of glucocorticoid receptor antagonist (GRA) sufficient to increase ACTH from the pituitary gland by at least two fold in persons with normal Hypothalamus Pituitary Adrenal (HPA) function;
>
> (iii) waiting for at least two hours; and,
>
> (iv) obtaining from the patient an ACTH concentration ratio wherein the ratio is derived from the ACTH concentrations in fluid obtained from either the left or right inferior petrosal venous sinus and from fluid obtained from a periphery venous sample.

Independent claim 18 is directed to a "method of concurrently treating Cushing's syndrome and obtaining a measurement indicative of differential diagnosis of adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome in a patient where the differential diagnosis is between ectopic ACTH syndrome and Cushing's disease." The method requires the steps of:

> determining the ACTH concentration ratio from a patient with Cushing's syndrome and an elevated ACTH level,
>
> where the patient has been administered a dose of glucocorticoid receptor antagonist (GRA) at least two hours prior to the removal of venous samples and

> where the amount of GRA administered to the patient is sufficient to increase ACTH from the pituitary gland by at least two fold in persons with normal Hypothalamus Pituitary Adrenal (HPA) function;
>
> wherein the ACTH concentration ratio is derived from the ACTH concentrations in fluid obtained from either the left or right inferior petrosal venous sinus and from fluid obtained from a periphery venous sample; and
>
> wherein an ACTH concentration ratio of greater than 3 for the ACTH concentration from the inferior venous sinus sample over the periphery venous sinus sample is indicative of Cushing's disease.

Teva's ANDA Product will not directly infringe claim 1 – either literally or under the doctrine of equivalents – Teva will not meet the limitations of "selecting a patient," much less a patient with Cushing's syndrome and elevated ACTH levels; Teva will not "administer[] a glucocorticoid receptor antagonist;" or wait for at least two hours and then "obtain[] from the patient an ACTH concentration ratio." Teva will not perform these steps because it will not diagnose patients taking Teva's ANDA Product. If an accused product or process lacks even one claim element, it does not literally infringe the claim. *Cross Med. Prods.*, 424 F.3d at 1310; *Pennwalt Corp.*, 833 F.2d at 935; and *Novartis Pharms. Corp.*, 363 F.3d at 1312. Because Teva does not perform any of these steps, Teva will not directly infringe claim 1.

Similarly, Teva will not directly infringe independent claim 18 – either literally or under the doctrine of equivalents – because Teva will not meet the limitation of "determining the ACTH concentration ratio from a patient with Cushing's syndrome and an elevated ACTH level." Teva will not perform this step because it does not and will not diagnose patients. If an accused product or process lacks even one claim element, it does not literally infringe the claim. *Cross Med. Prods.*, 424 F.3d at 1310; *Pennwalt Corp.*, 833 F.2d at 935; and *Novartis Pharms. Corp.*, 363 F.3d at 1312. Because Teva does not perform the step of "determining the ACTH concentration ratio," Teva will not directly infringe independent claim 18.

Furthermore, because Teva through its ANDA will not treat Cushing's syndrome and differentially diagnose (or obtain a measurement indicative of) adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome in patients, Teva through its ANDA will not infringe independent claims 1 and 18 of the '495 patent under the doctrine of equivalents. The doctrine of equivalents does not allow a claim limitation to be ignored. *Pennwalt Corp. v. Durand-Wayland, Inc.*, 833 F.2d 931, 935 (Fed. Cir. 1987); *see also Novartis Pharms. Corp. v. Eon Labs Mfg., Inc.*, 363 F.3d 1306, 1312 (Fed. Cir. 2004). Because Teva through its ANDA will not treat Cushing's syndrome and differentially diagnose (or obtain a measurement indicative of) adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome in patients, Teva will not, directly infringe independent claims 1 and 18 of the '495 patent, either literally or under the doctrine of equivalents.

Accordingly, Teva will not directly infringe claim 1-18 of the '495 patent, either literally or under the doctrine of equivalents.

1. No Inducement of Infringement

The proposed labeling for Teva's ANDA Product will not induce infringement of the claims of the '495 patent because the proposed labeling will not direct a person to "differentially diagnos[e] adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome in a patient where the differential diagnosis is between ectopic ACTH syndrome and Cushing's disease" (claims 1-17) or to "obtain[] a measurement indicative of differential diagnosis of adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome in a patient where the differential diagnosis is between ectopic ACTH syndrome and Cushing's disease" (claim 18). There are no instructions in the proposed labeling for Teva's ANDA Product directing that mifepristone should be, or even could be, used to differentially diagnose adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome in a patient where the differential diagnosis is between ectopic ACTH syndrome and Cushing's disease, or, for that matter, used in any diagnostic method.

Labeling that merely directs a person to administer Teva's ANDA Product "to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery"does not induce infringement of a method claim that involves administration of a glucocorticoid receptor antagonist to differentially diagnose adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome in a patient where the differential diagnosis is between ectopic ACTH syndrome and Cushing's disease. *See Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1364 (Fed. Cir. 2003); *see also Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316 (Fed. Cir. 2012). Thus, the proposed labeling for Teva's ANDA Product would not induce infringement of the claims of the '495 patent.

Furthermore, the proposed labeling for Teva's ANDA Product would not induce infringement of claims 8-17 of the '495 patent for the additional reason that claims 8-17 of the '495 patent require administering a glucocorticoid receptor antagonist falling within a genus of structures or having an expressly recited structure and the proposed labeling for Teva's ANDA Product does not instruct to administer a glucocorticoid receptor antagonist having a structure encompassed by these claims. Moreover, mifepristone is substantially different from, and, therefore, not equivalent to the glucocorticoid receptor antagonists of claims 8-17. *Abbott Labs. v. Novopharm Ltd.*, 323 F.3d 1324, 1329 (Fed. Cir. 2003) and *AquaTex Indus., Inc. v. Techniche Solutions*, 479 F.3d 1320, 1326 (Fed. Cir. 2007) (citing *Graver Tank & Mfg. Co. v. Linde Air Products Co.*, 339 U.S. 605, 608 (1950)). In particular, mifepristone has a different chemical formula and structure, and, thus, different chemical properties, from the genus of glucocorticoid receptor antagonists recited in claims 8-17. By separately claiming a method wherein mifepristone is the glucocorticoid receptor antagonist (*e.g.,* claim 7), Patentees of the '495 implicitly acknowledge that mifepristone is substantially different from the glucocorticoid receptor antagonist encompassed by claims 8-17. Labeling that directs a person to administer a glucocorticoid receptor antagonist having a structure that is different from the structure expressly recited in a claim does not induce infringement of a method of treatment claim that requires administering a glucocorticoid receptor antagonist having an expressly recited structure. *See Warner-Lambert Co.*, 316 F.3d at 1364; *Bayer Schering Pharma AG*, 676 F.3d at 1316.

Accordingly, the proposed labeling for Teva's ANDA Product would not induce infringement of the claims of the '495 patent.

2. No Contributory Infringement

Teva will not be liable for contributory infringement of the claims of the '495 patent because the Teva's ANDA Product would be a staple article of commerce clearly suitable for substantial uses that would not infringe the claims of the '495 patent, namely "to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery."

3. Dependent Claims 2-17

Claims 2-17 depend directly or indirectly from claim 1. Teva will not directly infringe dependent claims 2-17 of the '495 patent, either literally or under the doctrine of equivalents, at least by virtue of their dependence on independent claim 1. *Wahpeton Canvas Co. v. Frontier, Inc.*, 870 F.2d 1546, 1552 (Fed. Cir. 1989) ("It is axiomatic that dependent claims cannot be found infringed unless the claims from which they depend have been found to have been infringed").

4. Conclusions Regarding Non-Infringement

Accordingly, for the reasons set forth above, Teva's ANDA Product will not infringe the claims of the '495 patent, either literally or under the doctrine of equivalents.

VII. CONCLUSION

For the reasons discussed herein, each and every claim of U.S. Patent Nos. 8,921,348 and 9,829,495 are invalid, unenforceable and/or will not be infringed by the commercial manufacture, use or sale of Mifepristone Tablets, 300 mg product described in Teva's ANDA No. 211436.

As such, there is no reasonable basis upon which Corcept Therapeutics, Inc., as the apparent holder(s) of approved New Drug Application No. 202107 for KORLYM® (mifepristone) tablets 300 mg, and as the apparent record owner(s) of U.S. Patent Nos. 8,921,348 and 9,829,495, can institute suit against Teva for filing of its ANDA No. 211436, as the information provided herein makes clear.

Teva expressly reserves the right to develop and make other arguments and assert any defenses relating to non-infringement, invalidity and/or unenforceability of any or all of the claims of U.S. Patent Nos. 8,921,348 and 9,829,495.